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immunoglobulin heavy chain variable region framework is at least 70% identical to the sequence of the donor immunoglobulin heavy chain variable region framework.

E5

142. (New) A humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of 10^8 M^{-1} to 10^{10} M^{-1}, wherein the sequence of the humanized immunoglobulin heavy chain variable region framework is at least 70% identical to the sequence of the donor immunoglobulin heavy chain variable region framework and comprises at least 70 amino acids identical to an acceptor human immunoglobulin heavy chain variable region amino acid sequence.

REMARKS

The courtesies extended by the Examiner and Supervisory Examiner Feisee at the recent personal interview are acknowledged with appreciation. The following remarks set forth the contents of the interview, with the numbered sections in the Office Action addressed serially.

Before specifically addressing the Office Action, however, Applicants would like to direct the Examiner's attention to the "Patentee's Observations on the Arguments of the Opponents," which was filed in the previously discussed Opposition at the European Patent Office in the corresponding EP patent. (The Observations document is included in the IDS submitted concurrently with this Amendment.) Section A.2 of the Observations (beginning at page 5) restates the contributions underlying the present invention:

The invention claimed in the contested patent for the first time enabled a general approach to providing improved forms of humanized antibodies (immunoglobulins) that exhibit satisfactory binding capabilities while remaining substantially non-immunogenic in humans. The contested patent provides the essential technical teaching necessary for skilled persons easily and economically to produce such immunoglobulins for therapeutic formulation and other uses.

The present invention contributed a conceptual breakthrough which followed the realization by the inventors that the prior art methods were not, in fact, generally satisfactory for retaining high binding affinity in humanized antibodies. This contribution, the solution to the problem, can be expressed in a number of ways. Thus, the contribution can be expressed as substituting one or more amino acids in the antibody framework with corresponding amino acid(s) from the non-human donor immunoglobulin <u>in addition to</u> transferring complementarity determining regions (CDRs), taking due account, as in Cheetham and Riechmann et al., of the impact of both Kabat and Chothia. This contribution could, however, be equally well defined (the result being the same) in terms of transferring CDRs defined by Kabat together with substituting from the donor antibody those amino acids constituting the CDR H1 loop as defined by Chothia because they interact with the Kabat CDRs and, <u>in addition</u>, substituting one or more other amino acids outside the CDRs. This second way of expressing the contribution is reflected by the Example in the contested patent. In any event, either way of defining the contribution involves one or more amino acid substitutions in framework amino acid positions from the non-human donor antibody, which positions are outside the CDRs as defined by Kabat and Chothia. These positions were not candidates for change to donor amino acids in the contemplation of the prior art. The contested patent provides full information

on the choice of such amino acid substitutions in any given situation.... After this design phase, the task of generating any particular humanized immunoglobulin is routine work for the molecular biologist.

The breakthrough nature of the invention disclosed in the contested patent is demonstrated by the successful clinical development of the humanized anti-Tac antibody specifically described in the patent's Experimental Section. In each of two, multinational, placebo-controlled phase III clinical trials in kidney transplantation, treatment with humanized anti-Tac together with standard immunosuppressive drugs produced a statistically significant reduction in the incidence of acute rejection episodes within six months of transplant relative to standard immunosuppression alone.... In addition, when data from the two trials was pooled, at six months post-transplant there were 10 deaths and 31 transplanted kidneys lost in the placebo treated groups, but only 1 death and 16 transplants lost in the groups treated with humanized anti-Tac - a 90% reduction in mortality and approximately 50% reduction in kidney loss. There was no increase in serious adverse events due to humanized anti-Tac in the trials, <u>and no clinically significant HAMA response was observed</u>. On December 10, 1997, the U.S. Food and Drug Administration (FDA), acting on the unanimous endorsement of an advisory panel, granted marketing clearance for humanized anti-Tac (generic name, daclizumab; tradename, Zenapax®) which thus became the first humanized antibody approved for marketing anywhere in the world. In announcing the approval of this product, the FDA stated: "this new biotech product gives transplant patients and their doctors a new important weapon to fight kidney rejection." (Emphasis in original; reference numbers deleted.)

Support for Amendments

All of the elements in the pending claims, specifically including the claim amendments, are fully supported in the first (U.S.S.N. 290,975, filed December 28, 1988) and/or second (U.S.S.N. 310,252, filed February 13, 1989) priority applications. These two priority documents will be referred to as PDL I and PDL II, respectively; and it should be noted that PDL II incorporated by reference PDL I in its entirety (see, PDL II, page 1, lines 4-6).

So for example, support for the "70 amino acid residues" recitation added to claims 111 and 115 can be found in the subject specification at, e.g., page 64, line 9 and PDL I at page 10, lines 2-5.

Also, Claims 114, 118, 121 and 123 were amended to conform to the several other pending claims that recite the criteria "is capable of interacting with the CDRs." Support can be found in the subject specification at page 32, line 35 and in PDL II at, e.g., page 12, lines 33-34.

Support in Claims 119, 120, 121 and 126 for the recitation of "antibody tetramer, Fab, or $(Fab')_2$" can be found in the subject specification at page 26, lines 21-29 and in PDL I at page 8, lines 15-16 and page 9, lines 14-15.

Support in Claims 118, 122 and 123 for the language "is outside of Chothia CDR H1 (amino acids 26-32)" is based on the fact that the resultant claim scope is identical with defining the invention as changing amino acids "outside the Kabat and Chothia CDRs," as explained in more detail below.

Support in the new dependent Claims 139, 140 and 141 for the recitation of "70%" can be found in the subject specification at page 4, line 19 and in PDL II at page 3, line 22.

As noted, new Claims 136-141 are all fully based on the other already pending claims as amended and add no new matter.

Response to the Office Action by Section

1. The Examiner's comments in this section are not completely understood. Certain of the comments appear to refer to the subject matter of U.S. 5,530,101. As these comments are not specific to this case, a reply does not seem appropriate. In any event, the subsequent sections explain the present invention and contribution in detail.

2. The sequence disclosure will be the same as in previous issued applications, and will be provided under separate cover with a substitute specification.

3. The status of all parent applications has been amended as requested and will also be corrected in the substitute specification.

4-7. A substitute specification will be provided under separate cover as noted above.

8. Claims 111-135 are objected to as allegedly being indefinite on various grounds. Our review of the application indicates that claim 119 does not appear to have been objected to, and otherwise this objection is respectfully traversed.

8(a). First, claims 113 and 114 as currently amended recite Kabat and Chothia CDRs. Second, it is acknowledged that Claims 111, 112, and 115 do not recite a specific definition of CDRs but nonetheless do particularly point out and distinctly claim subject matter of the present invention. These claims are patterned after claims that were allowed and issued in U.S. 5,530,101 (see, e.g., claim 1) and U.S. 5,693,762 (see, e.g., claim 1), neither of which recites a CDR definition. An inventive concept of this claim type was based on the present

inventors' recognition that improved humanized antibodies could be obtained by first choosing an acceptor framework region with high homology to the donor framework. This comparison of framework regions is not dependent upon a CDR definition or CDR comparison and, thus, no such further limitations should be needed.

8(b). It is respectfully submitted that the affinity recitations are neither vague nor indefinite. Therefore, this objection is traversed. (The affinity recitations are discussed in detail in Section 9, below.)

8(c). Claim 115 has been amended to clarify that the humanized immunoglobulin also includes a light chain. Otherwise this objection is not understood, as each of claims 116-118 already recites a light chain.

8(d-f). Claims 111 and 115 have been amended as suggested.

8(g). Claims 124 and 125 have been amended to clarify reference to "donor" amino acids.

9. Various claims were also objected to under 35 U.S.C.§ 112, first paragraph. This objection is respectfully traversed.

9 (a & b). The Office Action alleges that the claims are directed to embodiments which may not have been enabled, such as humanized antibodies with significantly higher affinities than that of the donor antibody. Reference is made to the prior art, as well as the subject specifications showing comparable or slightly less affinity to the donor antibody. It is respectfully submitted, however, that these are just exemplary humanized antibodies and should not be considered limiting--particularly as the subject specification does disclose additional examples with significantly increased affinity over the donor. Subsequent publications by the inventors and others provide additional

evidence that skilled artisans were able to routinely practice the present invention and obtain humanized antibodies exhibiting increased affinity in comparison to the donor antibody.

As explained during the interview, humanized immunoglobulins made in accordance with the present invention have been shown experimentally to have affinities much stronger than their donor immunoglobulin. For example, both of the attached publications, Co et al. (1992) *J. Immunology* 148:1149-1154 and Caron et al. (1992) *Cancer Research* 52:6761-6767, describe humanized antibody affinities from about 3 to 8 fold stronger than the donor M195 antibody. Specifically, Co. et al. reported "about a 3-fold higher" affinity (see, bottom right hand column of page 1152 continued on page 1153). Similarly, Caron et al. reported the humanized antibodies "showed up to an 8.6- and 4-fold higher binding avidity" (see, Abstract, line 12). Both papers name original co-inventor Queen as an author, and describe humanized antibodies either precisely disclosed in the subject specification (e.g., humanized IgG_1, M195 described at specification pages 148-153) or otherwise made using the same humanized heavy chain variable domain with a different heavy chain constant domain (e.g., humanized IgG_3, M195; see, Co et al., page 1150, "Construction of expression vectors").

As another example which supports the findings of Caron et al. (1992), WO 96/05229 has specifically relied upon the teachings of the present invention to achieve humanized antibodies with affinity also reported to be about 8-fold higher than the donor mouse antibody. This patent application reports on the humanization of the mouse 1129 antibody (M1129) directed against the F glycoprotein of respiratory syncytial virus (RSV). In the final paragraph of page 9, the document states:

> In another embodiment, murine 1129 variable heavy chain was compared to various human variable region amino acids sequences, the highest homology was to the human

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> rearranged COR sequence. The two amino acid sequences were 75% homologous overall and 80% in the framework regions.... The murine derived variable heavy chain CDRs were then substituted into the variable heavy chain human COR V_H sequence.

Importantly, the details provided for making the humanized antibody follow <u>precisely</u> the method steps recited in, e.g., amended claim 1 of the present application (as well as Claim 14 of U.S. Patent No. 5,693,762, a related application). In particular, 80% homologous certainly satisfies the "at least 65%" criterion. In addition, examination of the 1129 antibody sequences in WO 96/05229 shows that the "at least 70 amino acids identical to an acceptor human immunoglobulin" feature is also present. Moreover, examination of Figure 7 of WO 96/05229 shows that the humanized 1129 antibody (designated H1129 or MEDI-493) comprises substitutions from the donor heavy chain framework outside the Kabat and Chothia CDRs, e.g., at position 85 (by Kabat numbering, or 90 by sequential numbering), where the "typical" amino acid Ala replaces the "rare" amino acid Tyr. Hence, this humanized antibody also supports the method disclosed in amended claim 120 of the present application.

Further, humanized antibody H1129 is reported in WO 96/05229 to have an affinity about 8-fold higher than the donor murine antibody M1129. Indeed, the table on page 29 states that K_d = 11.4 nM for M1129 and K_d = 1.4 nM for H1129. As the affinity (association) constant K_a is always the reciprocal of the dissociation constant K_d, this means that the affinity of M1129 is 8.8×10^7 M^{-1}, while the affinity of H1129 is 7.1×10^8 M^{-1}, about 8-fold greater.[1] Importantly, the applicants of WO 96/05229 did not do anything beyond the express teachings (particularly the criteria) of the present application to

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Applicants have not independently verified the data presented in WO 96/05229.

increase the affinity of the humanized antibody, i.e., they did not perform in vitro mutagenesis, affinity maturation, etc. On the contrary, they simply followed the criteria and other teachings of the present specification in a straightforward manner, which according to them yielded a humanized antibody with much greater affinity than the donor mouse antibody. In conclusion, the methods of the present application sometimes generate humanized antibodies with affinity slightly lower than the donor antibodies, more often with affinity essentially the same as the donor antibodies, sometimes with affinities higher but no greater than 4-fold, and sometimes with affinities even higher than that.

The subject specification sets out in particular detail those methods a skilled artisan can use to prepare humanized antibodies with acceptable affinities, including as amply demonstrated above, humanized antibodies with greatly increased affinities versus that of the donor. As pointed out above, those greater affinities were obtained without any additional experimentation to that detailed in the present specification. This evidence demonstrates unequivocally that the humanized antibodies of the present invention can exhibit affinities many fold greater than their respective donor antibodies. This objection should be reconsidered and the rejection withdrawn.

10(a). Various claims were also objected to under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification. The comments in the Office Action were not completely understood, however, the amendments to these claims obviate this objection.

Claim 114 has been amended to recite "outside the Kabat and Chothia CDRs." Claims 117, 118, 122 and 123 (and new claims 137 and 138), in which the replacing donor amino acids are specified as being from the heavy chain, have been amended to specify that the donor amino acids are "outside the Kabat CDRs" and "outside

Chothia CDR H1." It is submitted that this latter language is precisely equivalent to "outside the Kabat and Chothia CDRs." To wit, Chothia and Lesk, J. Mol. Biol. 196: 901 (1987), (which is incorporated by reference in PDL I at page 9, lines 4 - 6 and in the subject specification at, e.g., page 33, lines 23 to 26), list on page 904 the following alternative definitions of the heavy chain CDRs:

	Kabat	Chothia
H1	31 - 35	26 - 32
H2	50 - 65	53 - 55
H3	95 - 102	96 - 101

As may be seen from this table and is well understood, the Kabat CDRs H2 and H3 respectively contain the Chothia CDRs H2 and H3. Hence, a donor amino acid that is outside Kabat CDRs H2 and H3 is necessarily also outside these Chothia CDRs, and therefore outside these "Kabat and Chothia CDRs." Regarding the remaining heavy chain CDR, H1, a donor amino acid that is outside Kabat CDR H1 (31-35) and outside Chothia CDR H1 (26-32) must necessarily be outside the entire composite Kabat and Chothia CDR H1 (26-35). Thus, as stated, the two limitations "outside the Kabat CDRs" and "outside Chothia CDR H1" together have the same meaning as "outside the Kabat and Chothia CDRs." It is to be noted that the apposition "(amino acids 26-32)" inserted after "outside Chothia CDR H1" is for explicitness only, as Chothia CDR H1 means amino acids 26-32 as illustrated in the table above.

In view of the above, applicants request reconsideration and withdrawal of this rejection.

11. The support for the affinity limitations in U.S.S.N. 07/290,975 is acknowledged.

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12 & 13. Claims 111 and 115 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Riechmann et al., as evidenced by Cheetham. This rejection is respectfully traversed.

Simply stated, the Riechmann et al. humanized antibody and the mouse donor antibody do not show 65% identity between their heavy chain variable region frameworks, as recited in the noted claims. This can be readily seen by referring to the attached Appendix 1, which shows that the identity was only 55%. Therefore, Riechmann et al. does not anticipate any of the cited claims.

where?

Recently, it has been brought to Applicants' attention during the course of prosecution of the corresponding application in Japan that the framework of the humanized heavy chain described in Verhoeyen et al. (1988) *Science* 239: 1534-1536, (which is of record in the present application) may be 65.5% identical to the donor heavy chain variable region. This was not observed previously because the sequence of the donor antibody was not presented in Verhoeyen et al., and apparently was not published at the time, nor even at the priority dates of the present application.

Nonetheless, although several of the present claims recite " at least 65% identical," Verhoeyen et al. clearly does not anticipate any of these claims for at least the following reasons. First, all these claims require that both the heavy and light chains be humanized. See, e.g., clause (4) of claim 111, clause (4) of claim 115, and in claims 112 and 116 the phrase "humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chain frameworks." In contrast, Verhoeyen et al. reports an antibody in which only the heavy chain was humanized. Second, claims 112 and 116 require that the humanized immunoglobulin bind an antigen with an affinity

constant of at least 10^8 M^{-1}, while the affinity of the antibody in Verhoeyen et al. containing the humanized heavy chain is only about 2 x 10^7 M^{-1} (the K_d for the donor antibody is about 5 nM, so the affinity constant is the reciprocal of this or 2 x 10^8 M^{-1}, and the affinity of the humanized heavy chain-containing antibody is 10-fold less than that or 2 x 10^7 M^{-1}; see page 1535, first column, of Verhoeyen et al.). Finally, claims 111 and 115 recite the step of "(1) comparing the sequence of a donor immunoglobulin heavy chain variable region against a collection of sequences of human heavy chain variable regions." No such comparison is made or even suggested in Verhoeyen et al., where NEW was apparently chosen as the human acceptor sequence because its X-ray crystal structure was available, and. Apparently, it was only happenstance that high homology to the donor sequence significant homology existed.

Additionally, Verhoeyen et al., either alone or in combination with any other references of record, did not render the pending claims obvious under 35 U.S.C. Section 103(a). Verhoeyen et al. did not state that their humanized heavy chain was at least 65% identical to the donor framework. Nor could the skilled person have made this calculation when Verhoeyen et al. was published, nor even at the priority dates of the present application (including the immediately preceding application to the present divisional application, U.S.S.N, 634,278 filed December 19, 1990). Specifically, Verhoeyen et al. did not provide the sequence of the donor D1.3 antibody, which would have been needed to make such a calculation, rather citing it on page 1534, third column, as reference (7) "M.E. Verhoeyen, C. Berek, G. Winter, in preparation." A literature search using Medline of all publications by Verhoeyen did not identify any such manuscript providing the sequence of the donor D1.3 antibody was ever published. The D1.3 sequence was also not provided in the Fourth Edition (1987) of Kabat et. al., Sequences of Proteins of Immunological Interest, which is of record in the current case, and was first published in the Fifth Edition (1991), which cites

Verhoeyen, Berek, and Winter, *personal communication*, as the source.

Hence, it would only have been about 1991, after the priority dates of the present application, that the skilled person could in principle have determined the extent of identity between the donor and humanized D1.3 heavy chain frameworks. However, even had the D1.3 sequence been available earlier, the skilled person would have had no motivation to make this calculation or to learn anything from it. Indeed, nothing in the art prior to the present priority applications suggested that the extent of identity between the donor and acceptor or humanized heavy chain was in any way relevant to successful humanization. All three publications that disclosed humanized heavy chains before the priority dates, Riechmann et al., Verhoeyen et al. and Jones et al. (1986) *Nature* 321: 522 - 525, also of record, utilized the same NEW antibody to provide the human acceptor heavy chain framework, because of the availability of its X-ray structure (see Jones et al., page 523, lines 6-9). This resulted in various extents of identity between the respective donor and humanized heavy chains. There was no suggestion that it would be necessary or useful to choose a human acceptor variable region to increase the percent identity as presently claimed.

In conclusion, at the filing date of the present application, the person of ordinary skill in the art had neither means nor motivation to derive the 65% criterion of the pending claims, and therefore no ability to conceive the various steps of those methods to produce an immunoglobulin in which both the heavy and light chains were humanized and in which the heavy chain framework meets the specified criterion. This rejection should be withdrawn.

14-17. Various claims were further rejected under 35 U.S.C. Section 102(b) as being anticipated by, or in the alternative, under 35 U.S.C. Section 103 as obvious over Riechmann, as

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evidenced by Cheetham. This rejection is respectfully traversed.

As explained in previous responses and again at the interview, Riechmann et al.'s two amino acid changes at positions 27 and 30 of the heavy chain were within the Chothia CDR H1. This is contrary to the express requirement of the rejected claims. In fact, this was a basis that analogous claims in related patents were allowed, e.g., claim 4 of U.S. 5,585,089. The rejected claims are clearly distinguishable over and not suggested by Riechmann et al, and this rejection should be withdrawn.

In view of the foregoing, Applicants submit that all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (650) 326-2400.

Respectfully submitted,

J. Liebeschuetz

Joe Liebeschuetz
Reg. No. 37,505

For William M. Smith
Reg. No. 30,223

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
(650) 326-2400
Fax (650) 326-2422
WMS:tlg/jam/mos

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Appendix 1

Just to illustrate how silly 65% is as a homology here is the result of running the rat CD52 Campath heavy chain sequence against V-base. There are in fact 14 VH sequences greater than 65% homology overall not just for frameworks.

The total number of VH segments in V-base is 51 so this means that 14/51 are more than 65% homologous = 27.5% ie so more than 1/4 heavy chain VH sequences selected at random would meet the PDL 65% criteria! They claim that greater than 65% is 'unusually homologous" I would contest it is to be expected at a reasonable frequency.

Rat CD52 antibody (Campath-1G) run against V-Base

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Heavy Chain VH segment


Date: Thu, 9 Mar 2000 15:37:03 +0000

 TFASTA translates and searches a DNA sequence data bank
 version 3.2t07 August 17, 1999
Please cite:
 W.R. Pearson & D.J. Lipman PNAS (1988) 85:2444-2448

/tmp/.fasta3-search-5144071: 121 aa
 >cplgh
 vs  V-Base too library
searching /data/gcgblast/v-base 0 library
 167083 residues in   638 sequences
  Expectation_n fit: rho(ln(x))= 58.3236+/-0.0111; mu= -169.1206+/- 0.481;
 mean_var=11438.6422+/-9793.049, 0's: 1 Z-trim: 0  B-trim: 0 in 0/21
 Kolmogorov-Smirnov  statistic: 0.2425 (N=25) at  56

TFASTA (3.27 August, 1999) function [optimized, BL50 matrix (15:-5)] ktup: 2
 join: 36, opt: 36, gap-pen: -16/ -2, width:  16 reg.-scaled
 Scan time:  0.300
The best  scores are:                              initn init1 opt  z-sc E(637)
DP-34_DA-10                             ( 302) [1]  522   522  522   83.5    4.9
DP-29_12-2                              ( 302) [1]  511   511  511   82.5    5.6
VHD26                                   ( 302) [1]  483   483  483   79.8    7.7
DP-30                                   ( 302) [1]  479   479  479   79.5    8.1
V3-49                                   ( 302) [1]  469   469  476   79.2    8.4
HC15-7                                  ( 302) [1]  475   475  475   79.1    8.5
DP-57_HV3003-                           ( 302) [1]  465   465  473   78.9    8.7
DP-35_V3-11-                            ( 296) [1]  431   243  471   78.8    8.8
VH3-8                                   ( 294) [1]  441   253  469   78.7      9
LSG12-1                                 ( 302) [1]  463   463  470   78.6      9
DP-58_HV3D1EG                           ( 296) [1]  442   254  467   78.4    9.2
YAC-9_COS-27-                           ( 302) [1]  461   461  468   78.4    9.3
LSG6-1                                  ( 302) [1]  467   467  467   78.3    9.4
V3-22P                                  ( 302) [1]  455   455  463   78.0    9.8

>>DP-34_DA-10                                          (302 aa)
Frame: 1 initn: 522 init1: 522 opt: 522 Z-score: 83.5 expect()  4.9
 73.000% identity in 100 aa overlap (1-100:1-300)

               10        20        30        40        50        60
cplgh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.::::::::::::.:::::.:::::.:.::.:.::  ::. ::.::::.::.: ::
DP-34_  EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMSWVRQAPGKGLEWVGFIRNKANGGTT
          10        40        70        100       130       160

               70        80        90        100       110       120
cplgh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        : . :::::::::::..... :::::.:::::::.:::::
DP-34_  EXTTSVKGRFTISRDDSKSITYLQMNSLRAEDTAVYYCAR
          190       220       250       280


cplgh   S

>>DP-29_12-2                                           (302 aa)
Frame: 1 initn: 511 init1: 511 opt: 511 Z-score: 82.5 expect()  5.6
 72.000% identity in 100 aa overlap (1-100:1-300)

               10        20        30        40        50        60
cplgh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.::::::::::::.:::::.:::::.: ::.:.::  ::. ::.:   :.::..:::
DP-29_  EVQLVESGGGLVQPGGSLRLSCAASGFTFSDHYMDWVRQAPGKGLEWVGRTRNKANSYTT
          10        40        70        100       130       160

               70        80        90        100       110       120
cplgh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        ::  :::::::::::...: ::::::.:..::::.:::::
DP-29_  EYAASVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCAR
          190       220       250       280
```

3

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cp1gh  S

>>VHD26                                                   (302 aa)
Frame: 1 initn: 483 init1: 483 opt: 483 Z-score: 79.8 expect()  7.7
 69.000% identity in 100 aa overlap (1-100:1-300)

               10        20        30        40        50        60
cp1gh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.::::::::::::::.:::::.:::::.: ::.:.::  ::. : .:.::.::..:::
VHD26   EVQLLESGGGLVQPGGSLRLSCAASGFTFSDHYMSWVRQAQGKGLELVGLIRNKANSYTT
          10        40        70        100       130       160

               70        80        90        100       110       120
cp1gh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        ::  :::::.::::....: :::::..:..:: :.:::::
VHD26   EYAASVKGRLTISREDSKNTLYLQMSSLKTEDLAVYYCAR
         190       220       250       280


cp1gh  S

>>DP-30                                                   (302 aa)
Frame: 1 initn: 479 init1: 479 opt: 479 Z-score: 79.5 expect()  8.1
 68.000% identity in 100 aa overlap (1-100:1-300)

               10        20        30        40        50        60
cp1gh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.::::::::::::.:::::.:::::.: ::.:.::  ::. : .:.::.::..:::
DP-30   EVQLVESGGGLVQPGGSLRLSCAASGFTFSDHYMSWVRQAQGKGLELVGLIRNKANSYTT
          10        40        70        100       130       160

               70        80        90        100       110       120
cp1gh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        ::  :::::.::::....: :::::..:..:: :.:::::
DP-30   EYAASVKGRLTISREDSKNTLYLQMSSLKTEDLAVYYCAR
         190       220       250       280


cp1gh  S

>>V3-49                                                   (302 aa)
Frame: 1 initn: 469 init1: 469 opt: 476 Z-score: 79.2 expect()  8.4
 68.000% identity in 100 aa overlap (1-100:1-300)

               10        20        30        40        50        60
cp1gh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.:::::::::: :.::::..::::: :. :.:.::  ::. ::.::::.:: : ::
V3-49   EVQLVESGGGLVQPGRSLRLSCTASGFTFGDYAMSWFRQAPGKGLEWVGFIRSKAYGGTT
          10        40        70        100       130       160

               70        80        90        100       110       120
cp1gh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        ::. :::::::::::..... :::::.:..::::.:::.:
V3-49   EYTASVKGRFTISRDGSKSIAYLQMNSLKTEDTAVYYCTR
         190       220       250       280


cp1gh  S

>>HC15-7                                                  (302 aa)
Frame: 1 initn: 475 init1: 475 opt: 475 Z-score: 79.1 expect()  8.5
 67.000% identity in 100 aa overlap (1-100:1-300)

               10        20        30        40        50        60
cp1gh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.::::::::::::.:::::.:::::.: ::.:.::  ::. : .:.::.::..:::
HC15-7  EVQLVESGGGLVQPGGSLRLSCAASGFTFSDHYMSWVRQAQGKGLELVGLIRNKANSYTT
          10        40        70        100       130       160

               70        80        90        100       110       120
cp1gh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        ::  :::::.::::....: .::::..:..:: :.:::::
HC15-7  EYAASVKGRLTISREDSKNTMYLQMSNLKTEDLAVYYCAR
         190       220       250       280
```

```
cp1gh   S

>>DP-57_HV3003-                                        (302 aa)
Frame: 1 initn: 465 init1: 465 opt: 473 Z-score: 78.9 expect()  8.7
 67.000% identity in 100 aa overlap (1-100:1-300)

                10        20        30        40        50        60
cp1gh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.::::::::::::.:::::.:::::. .::. .::  ::. ::.::::.::.: ::
DP-57_  EVQLVESGGGLVQPGGSLRLSCAASGFTFSYYYMSGVRQAPGKGLEWVGFIRNKANGGTT
          10        40        70       100       130       160

                70        80        90       100       110       120
cp1gh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        : .  :::::::::::..... ::::.:.::::.::::.:
DP-57_  EXTTSVKGRFTISRDDSKSITYLQMKSLKTEDTAVYYCSR
         190       220       250       280


cp1gh   S

>>DP-35_V3-11-                                         (296 aa)
Frame: 1 initn: 431 init1: 243 opt: 471 Z-score: 78.8 expect()  8.8
 69.000% identity in 100 aa overlap (1-100:1-294)

                10        20        30        40        50        60
cp1gh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        .:.:.:::::::.::::.:::::.:::::.:.::.::::  ::. ::...:  ...: :
DP-35_  QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSYI--SSSGSTI
          10        40        70       100       130       160

                70        80        90       100       110       120
cp1gh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
         :  ::::::::::::..: ::::::.:::::::.:::::
DP-35_  YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
            190       220       250       280


cp1gh   S

>>VH3-8                                                (294 aa)
Frame: 1 initn: 441 init1: 253 opt: 469 Z-score: 78.7 expect()    9
 69.000% identity in 100 aa overlap (1-100:1-294)

                10        20        30        40        50        60
cp1gh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        .:.::::::::.::::.:::::.:::::.:.::.::::  ::. ::...: ....    :
VH3-8   QVQLLESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKGLEWVSYISSSSS--YT
          10        40        70       100       130       160

                70        80        90       100       110       120
cp1gh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        .:  ::::::::::::..: ::::::.:::::::.:::::
VH3-8   NYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
            190       220       250       280


cp1gh   S

>>LSG12-1                                              (302 aa)
Frame: 1 initn: 463 init1: 463 opt: 470 Z-score: 78.6 expect()    9
 67.000% identity in 100 aa overlap (1-100:1-300)

                10        20        30        40        50        60
cp1gh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.:::::::::: :.::::..:::::  . :.:.::  ::. ::.::::.:: : ::
LSG12-  EVQLVESGGGLVQPGPSLRLSCTASGFTFGYYPMSWVRQAPGKGLEWVGFIRSKAYGGTT
          10        40        70       100       130       160

                70        80        90       100       110       120
cp1gh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        ::  :::::::::::..... :::::.:..::::.:::.:
LSG12-  EYAASVKGRFTISRDDSKSIAYLQMNSLKTEDTAVYYCTR
         190       220       250       280
```

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```
cplgh  S

>>DP-58_HV3D1EG                                         (296 aa)
Frame: 1 initn: 442 init1: 254 opt: 467 Z-score: 78.4 expect()  9.2
 69.000% identity in 100 aa overlap (1-100:1-294)

                10        20        30        40        50        60
cplgh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.::::::::::::.:::::.:::::... :::.::  ::. ::...:  ...: :
DP-58_  EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYEMNWVRQAPGKGLEWVSYI--SSSGSTI
          10        40        70       100       130         160

                70        80        90       100       110       120
cplgh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
         :  ::::::::::::..: ::::::.:::::::.:::::
DP-58_  YYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR
           190       220       250       280


cplgh  S

>>YAC-9_COS-27-                                         (302 aa)
Frame: 1 initn: 461 init1: 461 opt: 468 Z-score: 78.4 expect()  9.3
 66.000% identity in 100 aa overlap (1-100:1-300)

                10        20        30        40        50        60
cplgh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.::::::::::::..::::.:::::.   :.:.:: .::. ::.: ::.::..:.:
YAC-9_  EVQLVESGGGLVQPGGSLKLSCAASGFTFSGSAMHWVRQASGKGLEWVGRIRSKANSYAT
          10        40        70       100       130       160

                70        80        90       100       110       120
cplgh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
         :  :::::::::::...:  :::::.:..::::.:::.:
YAC-9_  AYAASVKGRFTISRDDSKNTAYLQMNSLKTEDTAVYYCTR
         190       220       250       280


cplgh  S

>>LSG6-1                                                (302 aa)
Frame: 1 initn: 467 init1: 467 opt: 467 Z-score: 78.3 expect()  9.4
 66.327% identity in 98 aa overlap (1-98:1-294)

                10        20        30        40        50        60
cplgh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.:::::::.::::.:::::.:::::.. .:::.::  ::. ::.: :..:. : ::
LSG6-1  EVQLVESGGGLVKPGGSLRLSCAASGFTFSNAWMNWVRQAPGKGLEWVGRIKSKTDGGTT
          10        40        70       100       130       160

                70        80        90       100       110       120
cplgh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        .:   ::::::::::...: ::::::.:..::::.:::.
LSG6-1  DYAAPVKGRFTISRDDSKNTLYLQMNSLKTEDTAVYYCTT
         190       220       250       280


cplgh  S

>>V3-22P                                                (302 aa)
Frame: 1 initn: 455 init1: 455 opt: 463 Z-score: 78.0 expect()  9.8
 66.000% identity in 100 aa overlap (1-100:1-300)

                10        20        30        40        50        60
cplgh   EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTT
        ::.:.::::.:::::::.:::::.:::::. .::. .::  ::. ::.::::.::.: ::
V3-22P  EVHLVESGGALVQPGGSLRLSCAASGFTFSYYYMSGVRQAPGKGLEWVGFIRNKANGGTT
          10        40        70       100       130       160

                70        80        90       100       110       120
cplgh   EYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVS
        : . :::::::::::..... ::::..:..::::.:::.:
V3-22P  EXTTSVKGRFTISRDDSKSITYLQMKSLKTEDTAVYYCSR
         190       220       250       280
```

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cp1gh S

```
121 residues in 1 query   sequences
167083 residues in 638 library sequences
 Tcomplib (4 proc)[version 3.2t07 August 17, 1999]
 start: Thu Mar  9 15:37:02 2000 done: Thu Mar  9 15:37:03 2000
 Scan time:  0.300 Display time:  0.030

Function used was  TFASTA
```

Heavy Chain JH Segment

```
Date: Thu, 9 Mar 2000 18:09:31 +0000

 TFASTA translates and searches a DNA sequence data bank
 version 3.2t07 August 17, 1999
Please cite:
 W.R. Pearson & D.J. Lipman PNAS (1988) 85:2444-2448

/tmp/.fasta3-search-5508063: 21 aa
 >cp1ghj
 vs  V-Base too library
searching /data/gcgblast/v-base 0 library
 167083 residues in   638 sequences
  Expectation_n fit: rho(ln(x))= 3.9599+/-0.00831; mu= 1.2877+/- 0.468;
 mean_var=10.5398+/- 7.724, 0's: 2 Z-trim: 11  B-trim: 0 in 0/17
 Kolmogorov-Smirnov  statistic: 0.2173 (N=26) at  44

TFASTA (3.27 August, 1999) function [optimized, BL50 matrix (15:-5)] ktup: 2
 join: 36, opt: 36, gap-pen: -16/ -2, width:  16 reg.-scaled
 Scan time:  0.150
```

The best scores are:			initn	init1	opt	z-sc	E(625)
JH4D	(48)	[3]	90	90	90	276.0	9e-11
JH4B	(48)	[3]	90	90	90	276.0	9e-11
JH4A	(48)	[3]	90	90	90	276.0	9e-11
JH3B	(50)	[2]	85	85	85	260.1	6.9e-10
JH3A	(50)	[2]	85	85	85	260.1	6.9e-10
JH5A	(51)	[3]	80	80	80	244.5	5.2e-09
JH5B	(51)	[3]	79	79	79	241.4	7.6e-09
JH1	(52)	[1]	66	66	77	235.0	1.7e-08
JH2	(53)	[2]	75	75	75	228.6	3.9e-08
JH6A	(63)	[3]	62	62	69	208.0	5.5e-07
JH6B	(63)	[3]	62	62	69	208.0	5.5e-07
JH6C	(63)	[3]	57	57	64	192.6	4e-06

```
>>JH4D                                                    (48 aa)
Frame: 3 initn:  90 init1:  90 opt:  90 Z-score: 276.0 expect() 9e-11
 85.714% identity in 14 aa overlap (8-21:6-47)

                10        20
cp1ghj EGHTAAPFDYWGQGVMVTVSS
              :::::::..:::::
JH4D         YFDYWGQGTLVTVSS
                     30

>>JH4B                                                    (48 aa)
Frame: 3 initn:  90 init1:  90 opt:  90 Z-score: 276.0 expect() 9e-11
 85.714% identity in 14 aa overlap (8-21:6-47)

                10        20
cp1ghj EGHTAAPFDYWGQGVMVTVSS
              :::::::..:::::
JH4B         YFDYWGQGTLVTVSS
                     30
```

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```
>>JH4A                                                        (48 aa)
Frame: 3 initn:  90 init1:  90 opt:  90 Z-score: 276.0 expect() 9e-11
 85.714% identity in 14 aa overlap (8-21:6-47)

               10        20
cp1ghj EGHTAAPFDYWGQGVMVTVSS
              :::::::..:::::
JH4A         YFDYWGQGTLVTVSS
                     30

>>JH3B                                                        (50 aa)
Frame: 2 initn:  85 init1:  85 opt:  85 Z-score: 260.1 expect() 6.9e-10
 85.714% identity in 14 aa overlap (8-21:8-49)

               10        20
cp1ghj EGHTAAPFDYWGQGVMVTVSS
              :: ::::.::::::
JH3B        DAFDIWGQGTMVTVSS
                 20

>>JH3A                                                        (50 aa)
Frame: 2 initn:  85 init1:  85 opt:  85 Z-score: 260.1 expect() 6.9e-10
 85.714% identity in 14 aa overlap (8-21:8-49)

               10        20
cp1ghj EGHTAAPFDYWGQGVMVTVSS
              :: ::::.::::::
JH3A        DAFDVWGQGTMVTVSS
                 20

>>JH5A                                                        (51 aa)
Frame: 3 initn:  80 init1:  80 opt:  80 Z-score: 244.5 expect() 5.2e-09
 78.571% identity in 14 aa overlap (8-21:9-50)

               10        20
cp1ghj EGHTAAPFDYWGQGVMVTVSS
              :: ::::..:::::
JH5A        NWFDSWGQGTLVTVSS
                     30

>>JH5B                                                        (51 aa)
Frame: 3 initn:  79 init1:  79 opt:  79 Z-score: 241.4 expect() 7.6e-09
 78.571% identity in 14 aa overlap (8-21:9-50)

               10        20
cp1ghj EGHTAAPFDYWGQGVMVTVSS
              :: ::::..:::::
JH5B        NWFDPWGQGTLVTVSS
                     30

>>JH1                                                         (52 aa)
Frame: 1 initn:  66 init1:  66 opt:  77 Z-score: 235.0 expect() 1.7e-08
 64.706% identity in 17 aa overlap (5-21:1-51)

               10        20
cp1ghj EGHTAAPFDYWGQGVMVTVSS
           :  :..::::..:::::
JH1        AEYFQHWGQGTLVTVSS
            10        40

>>JH2                                                         (53 aa)
Frame: 2 initn:  75 init1:  75 opt:  75 Z-score: 228.6 expect() 3.9e-08
 71.429% identity in 14 aa overlap (8-21:11-52)

               10        20
cp1ghj EGHTAAPFDYWGQGVMVTVSS
              :: ::.:..:::::
JH2        YWYFDLWGRGTLVTVSS
                20        50

>>JH6A                                                        (63 aa)
Frame: 3 initn:  62 init1:  62 opt:  69 Z-score: 208.0 expect() 5.5e-07
 76.923% identity in 13 aa overlap (9-21:24-62)

               10        20
```

```
cplghj EGHTAAPFDYWGQGVMVTVSS
                : ::::. :::::
JH6A     YYYYYGMDVWGQGTTVTVSS
                 30         60

>>JH6B                                                      (63 aa)
Frame: 3 initn:  62 init1:  62 opt:  69 Z-score: 208.0 expect() 5.5e-07
 76.923% identity in 13 aa overlap (9-21:24-62)

                10         20
cplghj EGHTAAPFDYWGQGVMVTVSS
                : ::::. :::::
JH6B     YYYYYGMDVWGQGTTVTVSS
                 30         60

>>JH6C                                                      (63 aa)
Frame: 3 initn:  57 init1:  57 opt:  64 Z-score: 192.6 expect() 4e-06
 69.231% identity in 13 aa overlap (9-21:24-62)

                10         20
cplghj EGHTAAPFDYWGQGVMVTVSS
                : ::.:. :::::
JH6C     YYYYYYMDVWGKGTTVTVSS
                 30         60


21 residues in 1 query   sequences
167083 residues in 638 library sequences
 Tcomplib (4 proc)[version 3.2t07 August 17, 1999]
 start: Thu Mar  9 18:09:30 2000 done: Thu Mar  9 18:09:31 2000
 Scan time:  0.150 Display time:  0.020

Function used was  TFASTA
```

Light Chain VL segment

```
Date: Thu, 9 Mar 2000 15:38:26 +0000

 TFASTA translates and searches a DNA sequence data bank
 version 3.2t07 August 17, 1999
Please cite:
 W.R. Pearson & D.J. Lipman PNAS (1988) 85:2444-2448

/tmp/.fasta3-search-5216932: 108 aa
 >mrc7@cam.ac.uk
 vs  V-Base too library
searching /data/gcgblast/v-base 0 library

 167083 residues in   638 sequences
  Expectation_n fit: rho(ln(x))= 40.6350+/- 0.013; mu= -124.6895+/- 0.618;
 mean_var=10515.5456+/-9197.943, 0's: 1 Z-trim: 0  B-trim: 0 in 0/21
 Kolmogorov-Smirnov  statistic: 0.2044 (N=25) at  42

TFASTA (3.27 August, 1999) function [optimized, BL50 matrix (15:-5)] ktup: 2
 join: 36, opt: 36, gap-pen: -16/ -2, width:  16 reg.-scaled
 Scan time:  0.260
The best  scores are:
```

The best scores are:			initn	init1	opt	z-sc	E(637)
DPK1_018-	(287)	[1]	466	466	494	87.9	2.8
DPK9_012-	(287)	[1]	458	458	492	87.7	2.8
V3B	(287)	[1]	469	469	492	87.7	2.8
DPK4_A20	(287)	[1]	451	451	480	86.5	3.3
DPK8_VD	(287)	[1]	449	449	479	86.4	3.3
A30_SG3	(287)	[1]	462	462	473	85.9	3.6
V108	(287)	[1]	463	463	472	85.8	3.6
HK137	(287)	[1]	437	437	472	85.8	3.6
LFVK431	(287)	[1]	433	433	468	85.4	3.8
VB	(287)	[1]	439	439	468	85.4	3.8
DPK5_VB	(287)	[1]	439	439	468	85.4	3.8
DPK6_VB	(287)	[1]	439	439	468	85.4	3.8
DPK3_L11	(287)	[1]	451	451	466	85.2	3.9
DPK2_L14	(287)	[1]	444	444	464	85.0	4

```
Z4                                  ( 287) [1]  432  432  463   84.9     4.1
DPK7_HK134-                         ( 287) [1]  424  424  459   84.5     4.3
HK102_V1                            ( 287) [1]  433  433  459   84.5     4.3
DPK11_O14-                          ( 287) [1]  453  453  459   84.5     4.3
VA                                  ( 287) [1]  415  415  457   84.3     4.4
L12A_PCRDIL6-5                      ( 287) [1]  431  431  457   84.3     4.4

>>DPK1_O18-                                              (287 aa)
Frame: 1 initn: 466 init1: 466 opt: 494 Z-score: 87.9 expect()  2.8
 74.737% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cplgl   DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
        ::.:::::: ::::::::::..:.:::.:..::::::::: :..:::::::...::.::.::
DPK1_O  DIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPS
           10        40        70       100       130       160

               70        80        90       100
cplgl   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        ::::::::::::.::::::::::.:::.: :.  . :
DPK1_O  RFSGSGSGTDFTFTISSLQPEDIATYYCQQYDNLP
          190       220       250       280

>>DPK9_O12-                                              (287 aa)
Frame: 1 initn: 458 init1: 458 opt: 492 Z-score: 87.7 expect()  2.8
 75.789% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cplgl   DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
        ::.:::::: ::::::::::..:.:::.:..::::::::: :..:::::: ...::.:.::
DPK9_O  DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPS
           10        40        70       100       130       160

               70        80        90       100
cplgl   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        :::::::::::::::::::: :::.: :  : :
DPK9_O  RFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTP
          190       220       250       280

>>V3B                                                    (287 aa)
Frame: 1 initn: 469 init1: 469 opt: 492 Z-score: 87.7 expect()  2.8
 75.789% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cplgl   DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
        ::.:::::::::::::::::..:.:::.:..::::::::: :..:::::: ...::.:.::
V3B     DIQMTQSPSFLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPS
           10        40        70       100       130       160

               70        80        90       100
cplgl   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        :::::::::::::::::::: :::.:    : :
V3B     RFSGSGSGTDFTLTISSLQPEDFATYYCQCGYSTP
          190       220       250       280

>>DPK4_A20                                               (287 aa)
Frame: 1 initn: 451 init1: 451 opt: 480 Z-score: 86.5 expect()  3.3
 74.737% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cplgl   DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
        ::.:::::: ::::::::::..:.:::.:..:: ::::: :. :::::: ...::.:.::
DPK4_A  DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWYQQKPGKVPKLLIYAASTLQSGVPS
           10        40        70       100       130       160

               70        80        90       100
cplgl   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        :::::::::::::::::::::::::.: .. : :
DPK4_A  RFSGSGSGTDFTLTISSLQPEDVATYYCQKYNSAP
          190       220       250       280

>>DPK8_VD                                                (287 aa)
Frame: 1 initn: 449 init1: 449 opt: 479 Z-score: 86.4 expect()  3.3
 73.684% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
```

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```
cp1gl  DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
       ::..:::::::::::::::..:.:::.:..:: ::::: :.:::::: ...::.:.::
DPK8_V DIQLTQSPSFLSASVGDRVTITCRASQGISSYLAWYQQKPGKAPKLLIYAASTLQSGVPS
         10        40         70        100       130       160

              70        80        90        100
cp1gl  RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
       :::::::::.:::::::::::: :::.: :   : :
DPK8_V RFSGSGSGTEFTLTISSLQPEDFATYYCQQLNSYP
        190       220       250       280

>>A30_SG3                                               (287 aa)
Frame: 1 initn: 462 init1: 462 opt: 473 Z-score: 85.9 expect()  3.6
 73.684% identity in 95 aa overlap (1-95:1-285)

              10        20        30        40        50        60
cp1gl  DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
       ::.:::::: ::::::::::..:.::::.: . :.::::: :..:: ::: ...::.:.::
A30_SG DIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKRLIYAASSLQSGVPS
         10        40         70        100       130       160

              70        80        90        100
cp1gl  RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
       :::::::::.:::::::::::: :::.:::: : :
A30_SG RFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYP
        190       220       250       280

>>V108                                                  (287 aa)
Frame: 1 initn: 463 init1: 463 opt: 472 Z-score: 85.8 expect()  3.6
 72.632% identity in 95 aa overlap (1-95:1-285)

              10        20        30        40        50        60
cp1gl  DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
       ::..:::::: ::::::::::..:.::::.:.. :.::::: :..: :::: ...::.:.::
V108   DIQVTQSPSSLSASVGDRVTITCRASQGISNGLSWYQQKPGQAPTLLIYAASSLQSGVPS
         10        40         70        100       130       160

              70        80        90        100
cp1gl  RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
       :::::::::::::::::::::::::::.:::   . :
V108   RFSGSGSGTDFTLTISSLQPEDVATYYCLQDYTTP
        190       220       250       280

>>HK137                                                 (287 aa)
Frame: 1 initn: 437 init1: 437 opt: 472 Z-score: 85.8 expect()  3.6
 72.632% identity in 95 aa overlap (1-95:1-285)

              10        20        30        40        50        60
cp1gl  DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
       ::.:::::: ::::::::::..:.::::.:..:: :.::: :..:: ::: ...::.:.::
HK137  DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWFQQKPGKAPKSLIYAASSLQSGVPS
         10        40         70        100       130       160

              70        80        90        100
cp1gl  RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
       :::::::::::::::::::::: :::.: :. : :
HK137  RFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYP
        190       220       250       280

>>LFVK431                                               (287 aa)
Frame: 1 initn: 433 init1: 433 opt: 468 Z-score: 85.4 expect()  3.8
 71.579% identity in 95 aa overlap (1-95:1-285)

              10        20        30        40        50        60
cp1gl  DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
       ::.:::::: ::::::::::..:.::::.:..:: :.::: :..:: ::: ...::.:.::
LFVK43 DIQMTQSPSSLSASVGDRVTITCRASQGISNYLAWFQQKPGKAPKSLIYAASSLQSGVPS
         10        40         70        100       130       160

              70        80        90        100
cp1gl  RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
       .::::::::::::::::::::: :::.: :. : :
LFVK43 KFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYP
        190       220       250       280

>>VB                                                    (287 aa)
```

```
Frame: 1 initn: 439 init1: 439 opt: 468 Z-score: 85.4 expect()  3.8
 72.632% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cp1g1   DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
        ::.::::::: .::::::::::..:.:::.:...: ::::: :..::::::: ...::.:.::
VB      DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAASSLQSGVPS
          10        40        70        100       130       160

               70        80        90        100
cp1g1   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        :::::::::::::::::::::: :::.: :   : :
VB      RFSGSGSGTDFTLTISSLQPEDFATYYCQQANSFP
         190       220       250       280

>>DPK5_VB                                                  (287 aa)
Frame: 1 initn: 439 init1: 439 opt: 468 Z-score: 85.4 expect()  3.8
 72.632% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cp1g1   DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
        ::.::::::: .::::::::::..:.:::.:...: ::::: :..::::::: ...::.:.::
DPK5_V  DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAASSLQSGVPS
          10        40        70        100       130       160

               70        80        90        100
cp1g1   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        :::::::::::::::::::::: :::.: :   : :
DPK5_V  RFSGSGSGTDFTLTISSLQPEDFATYYCQQANSFP
         190       220       250       280

>>DPK6_VB                                                  (287 aa)
Frame: 1 initn: 439 init1: 439 opt: 468 Z-score: 85.4 expect()  3.8
 72.632% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cp1g1   DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
        ::.::::::: .::::::::::..:.:::.:...: ::::: :..::::::: ...::.:.::
DPK6_V  DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIYAASSLQSGVPS
          10        40        70        100       130       160

               70        80        90        100
cp1g1   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        :::::::::::::::::::::: :::.: :   : :
DPK6_V  RFSGSGSGTDFTLTISSLQPEDFATYYCQQANSFP
         190       220       250       280

>>DPK3_L11                                                 (287 aa)
Frame: 1 initn: 451 init1: 451 opt: 466 Z-score: 85.2 expect()  3.9
 73.404% identity in 94 aa overlap (2-95:4-285)

               10        20        30        40        50        60
cp1g1   DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
         :.::::::: ::::::::::..:.:::.: . :.::::: :..::::::: ...::.:.::
DPK3_L  AIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWYQQKPGKAPKLLIYAASSLQSGVPS
          10        40        70        100       130       160

               70        80        90        100
cp1g1   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        :::::::::::::::::::::: :::.:::   . :
DPK3_L  RFSGSGSGTDFTLTISSLQPEDFATYYCLQDYNYP
         190       220       250       280

>>DPK2_L14                                                 (287 aa)
Frame: 1 initn: 444 init1: 444 opt: 464 Z-score: 85.0 expect()    4
 70.526% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cp1g1   DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
        .:.:::::: .::::::::::..:.: :.:..:: :.::: :. :: ::: ...::.:.::
DPK2_L  NIQMTQSPSAMSASVGDRVTITCRARQGISNYLAWFQQKPGKVPKHLIYAASSLQSGVPS
          10        40        70        100       130       160

               70        80        90        100
cp1g1   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        ::::::::.::::::::::::: :::.:::: : :
```

```
DPK2_L RFSGSGSGTEFTLTISSLQPEDFATYYCLQHNSYP
         190       220       250       280

>>Z4                                                       (287 aa)
Frame: 1 initn: 432 init1: 432 opt: 463 Z-score: 84.9 expect()  4.1
 72.632% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cp1g1  DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
       ::.::::::: ::::::::::.:.::.:.. :::::: :.::.::: ..:.:.::::
Z4     DIQMTQSPSSLSASVGDRVTITCRASQGISNNLNWYQQKPGKTPKFLIYAASSLQSGIPS
         10        40        70        100       130       160

               70        80        90        100
cp1g1  RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
       ::: :::::::.:::::::::::: :::.: :  : :
Z4     RFSDSGSGTDYTLTISSLQPEDFATYYCQQSDSTP
         190       220       250       280

>>DPK7_HK134-                                              (287 aa)
Frame: 1 initn: 424 init1: 424 opt: 459 Z-score: 84.5 expect()  4.3
 71.579% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cp1g1  DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
       ::.::::::: ::::::::::.:.::::.:...: :::::  ..:: ::: ...::.:.::
DPK7_H DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQKPEKAPKSLIYAASSLQSGVPS
         10        40        70        100       130       160

               70        80        90        100
cp1g1  RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
       ::::::::::::::::::::::: ::::.: :. : :
DPK7_H RFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYP
         190       220       250       280

>>HK102_V1                                                 (287 aa)
Frame: 1 initn: 433 init1: 433 opt: 459 Z-score: 84.5 expect()  4.3
 70.968% identity in 93 aa overlap (1-93:1-279)

               10        20        30        40        50        60
cp1g1  DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
       ::.::::::: ::::::::::..:.:::.:...: ::::: :..:::::::....:..:.::
HK102_ DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYDASSLESGVPS
         10        40        70        100       130       160

               70        80        90        100
cp1g1  RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
       :::::::::.::::::::::::.: ::::.: :. :
HK102_ RFSGSGSGTEFTLTISSLQPDDFATYYCQQYNSYS
         190       220       250       280

>>DPK11_O14-                                               (287 aa)
Frame: 1 initn: 453 init1: 453 opt: 459 Z-score: 84.5 expect()  4.3
 71.579% identity in 95 aa overlap (1-95:1-285)

               10        20        30        40        50        60
cp1g1  DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
       ::..:::::: ::::::::::.:.:..::.:..:::::::.:: :. ::::::...:::.:.::
DPK11_ DIQLTQSPSSLSASVGDRVTITCRVSQGISSYLNWYRQKPGKVPKLLIYSASNLQSGVPS
         10        40        70        100       130       160

               70        80        90        100
cp1g1  RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
       ::::::::::::::::::::::::::::.  .  . :
DPK11_ RFSGSGSGTDFTLTISSLQPEDVATYYGQRTYNAP
         190       220       250       280

>>VA                                                       (287 aa)
Frame: 1 initn: 415 init1: 415 opt: 457 Z-score: 84.3 expect()  4.4
 71.277% identity in 94 aa overlap (2-95:4-285)

               10        20        30        40        50        60
cp1g1  DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
        :..:::::: ::::::::::..:.:::.:.. : ::::: :..:::::::....:..:.::
VA     AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLIYDASSLESGVPS
         10        40        70        100       130       160
```

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```
              70        80        90       100
cp1gl   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        :::::::::::::::::::::: :::.: :   : :
VA      RFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYP
         190       220       250       280

>>L12A_PCRDIL6-5                                        (287 aa)
Frame: 1 initn: 431 init1: 431 opt: 457 Z-score: 84.3 expect()  4.4
 70.968% identity in 93 aa overlap (1-93:1-279)

              10        20        30        40        50        60
cp1gl   DIKMTQSPSFLSASVGDRVTLNCKASQNIDKYLNWYQQKLGESPKLLIYNTNNLQTGIPS
        ::.:::::: :::::::::::..:.:::.:...: ::::: :..::::::....:..:.::
L12A_P  DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS
          10        40        70       100       130       160

              70        80        90       100
cp1gl   RFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRPRTFGTGTKLELKR
        :::::::::.::::::::::::.: :::.: :. :
L12A_P  RFSGSGSGTEFTLTISSLQPDDFATYYCQQYNSYS
          190       220       250       280


108 residues in 1 query   sequences
167083 residues in 638 library sequences
 Tcomplib (4 proc)[version 3.2t07 August 17, 1999]
 start: Thu Mar  9 15:38:26 2000 done: Thu Mar  9 15:38:26 2000
 Scan time:  0.260 Display time:  0.030

Function used was  TFASTA


Light Chain JK segment


Date: Thu, 9 Mar 2000 18:11:04 +0000

 TFASTA translates and searches a DNA sequence data bank
 version 3.2t07 August 17, 1999
Please cite:
 W.R. Pearson & D.J. Lipman PNAS (1988) 85:2444-2448

/tmp/.fasta3-search-5147508: 13 aa
 >cp1glj
 vs  V-Base too library
searching /data/gcgblast/v-base 0 library
 167083 residues in   638 sequences
  Expectation_n fit: rho(ln(x))= 1.4627+/-0.00917; mu= 9.2358+/- 0.518;
 mean_var=11.2187+/- 8.682, 0's: 18 Z-trim: 6  B-trim: 8 in 1/18
 Kolmogorov-Smirnov  statistic: 0.1797 (N=21) at  58

TFASTA (3.27 August, 1999) function [optimized, BL50 matrix (15:-5)] ktup: 2
 join: 36, opt: 36, gap-pen: -16/ -2, width:  16 reg.-scaled
 Scan time:  0.130
The best  scores are:                             initn init1 opt z-sc E(614)
JK2                                      ( 39) [3]   50    50   58  179.6 2.1e-05
JK5                                      ( 38) [2]   47    47   55  170.7 6.5e-05
JK1                                      ( 38) [2]   39    39   54  167.8 9.5e-05
JK4                                      ( 38) [2]   38    38   53  164.8 0.00014
JK3                                      ( 38) [2]   39    39   50  155.8 0.00044

>>JK2                                                   (39 aa)
Frame: 3 initn:  50 init1:  50 opt:  58 Z-score: 179.6 expect() 2.1e-05
 81.818% identity in 11 aa overlap (2-12:6-38)

              10
cp1glj RTFGTGTKLELKR
        ::: ::::::.:
JK2     YTFGQGTKLEIK
              30

>>JK5                                                   (38 aa)
Frame: 2 initn:  47 init1:  47 opt:  55 Z-score: 170.7 expect() 6.5e-05
```